

What is Claimed:

1. A non-natural heteropolymeric pulmonary spreading agent comprising at least one N-substituted glycine residue and at least one amino acid residue corresponding to a natural surfactant-associated protein, said protein selected from the group consisting of surfactant-associated protein B and surfactant-associated protein C.

2. The spreading agent of claim 1 wherein said N-substituent is a moiety selected from the group consisting of carbon homologs to the  $\alpha$ -carbon moieties of naturally-occurring  $\alpha$ -substituted amino acids.

3. The spreading agent of claim 1 wherein said protein is surfactant-associated protein B and residues 1-25 thereof.

4. The spreading agent of claim 3 wherein said residues are interspersed with said glycine residues.

5. The spreading agent of claim 3 wherein said surfactant-associated protein B residues comprise at least 70% of said spreading agent.

6. The spreading agent of claim 1 wherein said protein is surfactant-associated protein C and residues 1-35 thereof.

7. The spreading agent of claim 1 wherein said surfactant-associated protein C residues are 5-32.

8. The spreading agent of claim 7 wherein said surfactant-associated protein C residues comprise at least 70% of said spreading agent.

9. A pulmonary surfactant composition comprising a non-natural heteropolymeric spreading agent having at least one N-substituted glycine residue and at least one amino acid residue corresponding to a natural surfactant associated protein, said protein selected from the group consisting of surfactant-associated protein B and surfactant-associated protein C; and a component selected from the group consisting of naturally-occurring phospholipid, non-natural analogs of said phospholipids, commercial surface-active agents and combinations thereof, said composition having physiological alveolar surface activity.

10. The surfactant composition of claim 9 wherein said phospholipid is selected from the group consisting of dipalmitoylphosphatidylcholine,

phosphatidylcholine, phosphatidylglycerol, phosphatidylethanolamine, phosphatidylinositol, phosphatidylserine, and combinations thereof.

11. The surfactant composition of claim 9 further including a palmitic acid.
12. The surfactant composition of claim 9 wherein said spreading agent is present at about one weight percent to about twenty weight percent of said composition, and said phospholipid is present in an amount sufficient to reduce alveolar surface tension.
13. The spreading agent of claim 9 wherein said N-substituent is a moiety selected from the group consisting of carbon homologs to the  $\alpha$ -carbon moieties of naturally-occurring  $\alpha$ -substituted amino acids.
14. The spreading agent of claim 9 wherein said protein is surfactant-associated protein B and residues 1-25 thereof.
15. The spreading agent of claim 14 wherein said residues are interspersed with said glycine residues.
16. The spreading agent of claim 9 wherein said protein is surfactant-associated protein C and residues 1-35 thereof.
17. The spreading agent of claim 16 wherein said surfactant-associated protein C residues are 5-32.
18. A method of using N-substituent to enhance conformational control of a surfactant-associated protein mimic compound, said method comprising preparing a surfactant-associated protein mimic composition having at least one glycine residue, said preparation providing N-substituent of said glycine residue sufficient to enhance helical conformation of said composition.
19. The method of claim 18 wherein said N-substitution is a moiety selected from the group consisting of carbon homologs to the  $\alpha$ -carbon moieties of naturally-occurring  $\alpha$ -substituted amino acids.
20. The method of claim 18 wherein N-substitution provides a substituent selected from the group of moieties provided in figures 7a-7c.
21. The method of claim 18 wherein said protein mimic compound further includes at least one amino acid residue corresponding to a natural surfactant-associated

protein, said protein selected from the group consisting of surfactant-associated protein B and surfactant-associated protein C.

22. A method for controlling alveolar surface activity, said method comprising:

preparing a pulmonary surfactant composition including a non-natural heteropolymeric spreading agent having at one N-substituted glycine residue, and a lipid admixture; and

administering said composition in an amount sufficient to reduce alveolar surface tension.

23. The method of claim 22 wherein said spreading agent further includes at least one amino acid residue corresponding to a natural surfactant-associated protein selected from the group consisting of surfactant-associated protein B and surfactant-associated protein C, and said lipid admixture comprises components selected from the group consisting of naturally-occurring phospholipids, non-natural analogs of said phospholipids and combinations thereof.

24. A method of using N-substitution to enhance the solubility of a helical surfactant-associated protein mimic compound, said method comprising preparing a helical, monomeric surfactant-associated protein mimic compound having at least one glycine residue, said preparation providing N-substitution of said glycine residue sufficient to maintain said monomeric compound and increase the solubility of said compound.

25. The method of claim 24 wherein said mimic compound further includes at least one amino acid residue corresponding to a natural surfactant-associated protein selected from the group consisting of surfactant-associated protein B and surfactant-associated protein C.

26. A method of using a polypeptoid to affect alveolar surface tension during an inhalation/exhalation cycle, said method comprising:

providing a polypeptoid component consistent of a plurality of N-substituted glycine residues;

combining said polypeptoid component with a surface-active lipid admixture, said combination having biomimetic alveolar surface activity; and

administering said polypeptoid/lipid combination in an amount sufficient to reduce alveolar surface tension.

27. The method of claim 26 wherein said lipid admixture includes dipalmitoylphosphatidylcholine and dipalmitoylphosphatidylglycerol.

28. A pulmonary surfactant composition, comprising:  
a non-natural heteropolymeric spreading agent having the one-letter code structure



wherein  $\text{X}_1$  and  $\text{X}_2$  are selected from the group consisting of an F residue and a C-palmitoyl residue, wherein  $\text{NX}_3$  is an N-substituted polypeptoid with  $\text{X}_3$  selected from the group consisting of ssb and spe substituents, and wherein  $n$  is an integer from about 13-20; and

a lipid admixture combined with said spreading agent.

29. The surfactant composition of claim 28 wherein  $n$  is 15-16.

30. A pulmonary surfactant composition, comprising:  
a non-natural heteropolymeric spreading agent having the three-letter code structure



wherein  $\text{X}_1$  and  $\text{X}_2$  are selected from the group consisting of  $\text{Npm}$ ,  $\text{Noc}$  and  $\text{Mhd}$  substituted glycine residues, wherein  $\text{NX}_3$  is an N-substituted polypeptoid with  $\text{X}_3$  selected from the group consisting of spe and ssb substituents, and wherein  $n$  is an integer from about 13-20; and

a lipid admixture combined with said spreading agent.

31. The surfactant composition of claim 30 wherein  $n$  is 15-16.